sufficiently to produce labeled probe DNA hybridizable [essentially] specifically to the target chromosomal DNA.

29. (Amended) The method of claim 22, for simultaneous detection of more than one chromosome, or region, thereof, wherein the probe DNA for each chromosome, or region thereof, is labeled with or labelable with a different fluorophore or a different combination of fluorophores to yield optically distinguishable signals.

30. (Amended) A method of *in situ* hybridization for distinguishably labeling individual human chromosomes, or regions thereof, in interphase cells comprising:

a) providing labeled probe DNA for each chromosome, or region thereof, to be visualized, each probe having sequences specifically hybridizable to target chromosomal DNA, but having repetitive sequences which cross-hybridize to non-target chromosomal DNA and each probe DNA being labeled with or labelable with a different fluorophore or a different combination of fluorophores to generate optically distinguishable signals; and

b) combining
i) the labeled probe DNA for each chromosome, or region thereof;
ii) a competitor DNA containing the repetitive sequences; and
iii) a sample of interphase cells, or nuclei thereof, treated to render chromosomal DNA therein available for hybridization with the labeled probe DNA,

under hybridization conditions wherein cross-hybridization between repetitive sequences in the probe DNA and the sample is sufficiently suppressed to allow the probe DNA to hybridize [essentially] specifically to the target chromosomal DNA, to thereby distinguishably label individual chromosomes.

31. (Amended) A method of *in situ* hybridization for visualizing an individual human chromosome, or region thereof, in interphase cells comprising

a) providing biotinylated DNA fragments smaller than 500 nucleotides derived from a DNA library of a target chromosome, or region thereof, for visualization;

b) combining biotin-labeled DNA fragments with fragments of total genomic DNA having the same size distribution as the labeled fragments and incubating the mixture under initial conditions that allow denaturation of the fragments and, subsequently, under conditions that promote annealing of fragments containing repetitive sequences but not fragments containing chromosome-specific sequences, to produce probe DNA [essentially] specific for the target chromosome;

c) combining the probe DNA with a [cellular preparation] sample of interphase cells, or nuclei thereof, treated to render target chromosomal DNA available for hybridization with the probe DNA, under conditions which allow the probe DNA to hybridize to the target chromosomal DNA; and

d) visualizing the individual human chromosome, or region thereof, by detecting the probe DNA by incubating the preparation with an avidin conjugated fluorophore and the detection of the fluorescent signal.

32. (Amended) A method of *in situ* hybridization for simultaneously visualizing individual human chromosomes, or regions thereof, in interphase cells comprising

a) providing labeled probe DNA for each chromosome, or region thereof, to be visualized, each probe DNA having sequences specifically hybridizable to target chromosomal DNA, but having repetitive sequences which cross-hybridize to non-target chromosomal DNA and each probe DNA being labeled with or labelable with a different fluorophore or a different combination of fluorophores to generate optically distinguishable signals;

b) combining

i) the labeled probe DNA for each chromosome, or region thereof;

ii) a competitor DNA containing the repetitive sequences; and

iii) a sample of interphase cells, or nuclei thereof, treated to render chromosomal DNA therein available for hybridization with the labeled probe DNA, under hybridization conditions wherein cross-hybridization between repetitive sequences in the probe DNA and the sample is sufficiently suppressed

to allow each probe DNA to hybridize [essentially] specifically to the target chromosomal DNA; and

c) detecting the optically distinguishable signals generated by each probe DNA to simultaneously visualize each chromosome.

33. (Amended) A method according to claim 32, wherein the detecting step includes the step of

a) generating one or more digital images of the hybridized chromosomal DNA; and

b) visually emphasizing those portions of the digital images which represent optically distinguishable signals associated with a [fluorophor] fluorophore or combination thereof.

35. (Amended) A method according to claim 34, wherein the visually emphasizing step includes the steps of generating an image of the hybridized chromosomal DNA by

a) assigning a respective color to each [fluorophor] fluorophore; and

b) substituting, for those portions of the digital images which represent optically distinguishable signals associated with the [fluorophors] fluorophores, or combinations thereof, respective colors assigned thereto.

REMARKS

The above amendments and following remarks are directed to rejections which remained outstanding in an Action (Paper No. 31) dated December 23, 1993 issued in U.S. Serial No. 07/837,664, of which this application is a File Wrapper Continuation.

The Brief Description of the Drawings in the specification has been amended to correctly identify the figures as suggested by the Examiner in the Action of December 23, 1993 issued in U.S. Serial No. 07/837,664. The amendment of the Brief Description of the Drawings submitted herewith is intended to replace the amendment of the Brief Description of the Drawings filed on September 20, 1993 in U.S. Serial No. 07/837,664.